Tertiary Quaternary Drug List
Medication Review Summary

Date: July 2018

Medication Name: Rituximab

Indications: Treatment of refractory rheumatoid arthritis (RA) in patients with an inadequate response to multiple synthetic disease-modifying anti-rheumatic drugs (sDMARDs).

Context: RA is the most common cause of inflammatory, destructive arthritis in adults and is a major cause of musculoskeletal disability. Prevalence rates for RA range from 0.1-1 % of the adult population. Patients in whom sDMARDS fail to adequately control RA, it can usually be controlled with biological DMARDs, including agents such as TNF-α inhibitors, abatacept, tocilizumab and rituximab.

Evidence synthesis: In a Cochrane Review[1] including eight randomised controlled trials, rituximab in combination with methotrexate was shown to improves outcomes as measured by a variety of validated disease activities indices:

- American College of Rheumatology (ACR) response of ≥50%: at 24 weeks absolute treatment benefit 21% (95% CI 16%-25%), NNT = 6 (95% CI 9 – 4).
- 28 Joint Disease Activity Score (DAS28), clinical remission: at 52 weeks, absolute treatment benefit 11% (95% CI 2%-20%), NNT = 7 (95% CI 13 – 4).
- Radiographic progression: at 24 weeks, absolute treatment benefit 11% (95% CI 2%-19%), NNT = 10 (95% CI 5 – 57). Similar results at 52 and 104 weeks.

Two treatment regimens have been tested in patients with RA, namely two cycles of 1000 mg (separated by two weeks) or two cycles of 500 mg (separated by two weeks) at 6-monthly intervals, respectively, and these have been demonstrated to be equally effective in controlling disease activity[2].

Safety concerns: Prolonged B-cell depletion with associated greater infection risk.

Cost

Medicine	Ave Cost per annum/patient	Annual budget impact
Triple Therapy	R 3,759.96	R 37,599,600.00
Rituximab plus methotrexate	R 33,488.04	R 33,909,816.00

The projected budget impact of adding rituximab in RA for refractory patients (~10% of RA patients), would be about 33 million (based on current contract prices, December 2017)

Recommendation: In the South African context Rituximab (in combination with methotrexate) is recommended as a bDMARD for refractory RA and should be considered in patients, who have failed treatment with ≥ 3 sDMARDs taken for ≥6 months[3] for refractory RA on a **named-patient** basis approved by Pharmacy and Therapeutics Committee. The recommended dose is 2 x 500 mg cycles, 6-monthly. *(See RA algorithm)*

References:

[1]Lopez-Olivo MA, Amezaga Urruela M, McGahan L, Pollono EN, Suarez-Almazor ME . Rituximab for rheumatoid arthritis. Cochrane Database Syst Rev. 2015 Jan 20;1:CD007356. doi: 10.1002/14651858.CD007356.

[2] Rubbert-Roth A, Tak PP, Zerbini C, *et al*. Efficacy and safety of various repeat treatment dosing regimens of rituximab in patients with active rheumatoid arthritis: results of a Phase III randomized study (MIRROR). Rheumatology 2010; 49:1683–1693.

[3] Tikly M, Hodkinson B, Dheda K. Biologic therapy for rheumatoid arthritis in developing countries – a place for non-TNF inhibitors as first line treatment? Rheumatology 2015; 54: 208-209.